Rate Control of Atrial Arrhythmias Can Be Achieved by Selective Cardiac Neurostimulation

Mark Marchitto, BS, Aditya C. Sharma, MD, Jeffrey P. Moak, MD, Dingchao He, MD, Conor Hynes, MD, Gregory Trachiotis, MD, Andy Blichard, BS, Erin Montague, BS, Xiyan Li, BS, Gene Bornzin, PhD, FHRS, Charles I. Berul, MD, FHRS, Richard Jonas, MD, and Marco A. Mercader, MD, FHRS.

George Washington University - Cardiology, Washington, DC, Children's National Medical Center - Dept. of Cardiology, Washington, DC, Children's National Medical Center - Surgery, Washington, DC, George Washington University - Surgery, Washington, DC, Georgetown University, Washington, DC, St. Jude Medical, Sylmar, CA

Introduction

Supraventricular arrhythmias, such as junctional ectopic tachycardia (JET) and atrial fibrillation (AF), frequently complicate recovery from open-heart surgery in children and can be difficult to manage using current approaches. Pharmacologic treatment has been the main strategy for the control of post-operative atrial arrhythmias (AA), but is associated with hypotension, pro-arrhythmia and myocardial dysfunction. There is a need for a reversible, modulated solution to rate control. We propose a non-pharmacologic technique that can modulate AV nodal conduction and automaticity, while still allowing the natural function of the electrical system. In our canine model, direct stimulation of the AV nodal Fat Pad using our novel catheter and control device has been shown to result in rate control acutely.

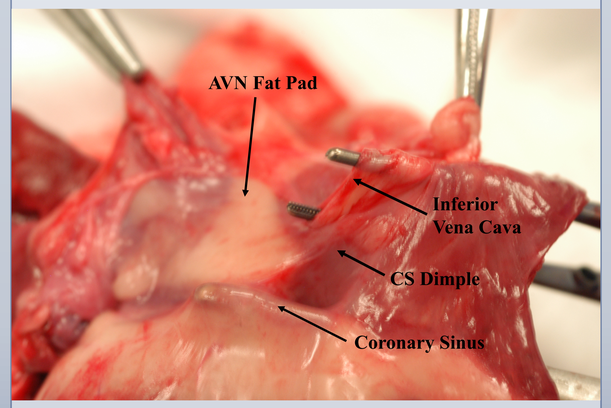

Figure 1. Right inferior AV node fat pad. Shown is the posterior wall of the heart from a postmortem dog. Illustrated and labeled in the center of the image is the right inferior AV node fat pad, which is located at the junction of the inferior vena cava, coronary sinus (CS), and right lower pulmonary vein. Our neural stimulating electrode was sewn to this region of the atrium.

We demonstrated the efficacy of vagal stimulation at the inferior right fat pad (FP) to slow the ventricular response (VR) of AF and JET. We hypothesized that the VR response to AA could be improved by alterations in 1) the site of stimulation (anterior right FP vs. inferior right FP), 2) site within the two FP regions tested, and 3) whether there was a relationship between stimulation voltage (V) and electrophysiologic effect.

Methods

Eight mongrel dogs, age 8.7 ± 3.9 months and weighing 21.5 ± 2.5 kg, underwent open heart surgery replicating Tetralogy of Fallot repair. Stimulation of the anterior right (AR) and inferior right (IR) fat pad was used to control the VR of AF and JET. A 7-pole electrode was sutured to the AR and IR FP and used to deliver stimulation therapy. Tested parameters included: 1) FP site, 2) stimulation pole configuration, and 3) stimulation (1-25) V on the VR to AF and JET. Stimulation frequency was 30 Hz, and pulse width was 0.15 msec.

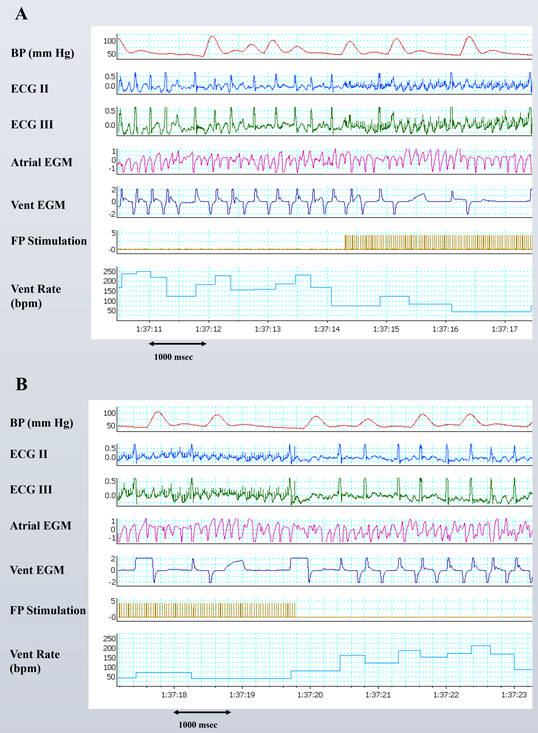

Figure 2. Effect of fat pad (FP) stimulation during atrial fibrillation on the ventricular (Vent) rate response. **A**, Onset of FP stimulation. The atrial electrogram (EGM) revealed continuous and fragmented electric activity consistent with persistent atrial fibrillation. Evident on review of ECG leads II and III was a rapid and irregular Vent response to the atrial fibrillation. After AV nodal FP stimulation, the Vent rate significantly slowed from ≈200 to 75 beats per minute. Accompanying electric slowing of the Vent rate was correction of the electric-mechanical pulse deficit. **B**, Termination of FP stimulation. After termination of FP stimulation, as indicated by the absence of activity on the FP stimulation channel, the Vent rate increased back to baseline.

Results

1). The inferior right FP was more effective in slowing the VR response to AF (-0.43 ± 0.18 vs. -0.18 ± 0.11 %, p =0.03) and JET (-0.16 ± 0.06 vs. 0.0 ±0.0, p =0.06.) 2). Selective site stimulation within a FP region could augment the effect of stimulation during AF (-0.48 ± 0.21 (maximum effect) vs. 0.0 ± 0.0 % (least effect), p=0.01). Stimulation of electrodes 2+3 produced the greatest reduction in HR with a maximum percent VR reduction of 34.8% 3). FP stimulation at increasing V demonstrated a voltage-dependent effect (-0.12 ± 0.19 (low V) vs. -0.63 ± 0.21 (high V) %, p=0.01).

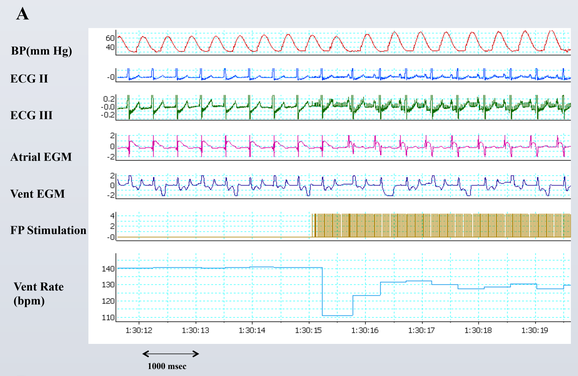

Figure 3. Effect of fat pad (FP) stimulation during junctional ectopic tachycardia (JET). **A**, Onset of FP stimulation. JET was present before the onset of FP stimulation and was evident on the left-hand side of the figure. No P waves are observed preceding the QRS and there was simultaneous occurrence of the atrial and ventricular (Vent) electrograms (EGM). After the onset of FP stimulation, the Vent rate slowed, and the atrial and Vent EGM separated, with the atrial EGM preceding the Vent EGM, indicating the development of sinus rhythm. An increase in the systolic blood pressure accompanied the develop- ment of sinus rhythm. **B**, Termination of FP stimulation. When AV node FP stimulation was terminated, indicated by the cessation of activity on the FP stimulation channel, sinus rhythm gradual transi- tioned back to JET and was accompanied by an increase in the Vent rate and a decline in the systolic blood pressure.

Conclusions

Selective site stimulation within a fat pad region and optimizing the voltage output enhanced the efficacy of ventricular rate (VR) slowing during post-op AA. Stimulating multiple sites of the inferior right fat pad using combinations of electrodes allowed for maximal slowing of VR. The inferior right fat pad was more effective in decreasing VR during AF, suggesting its role in control of AV node conduction. The anterior right fat pad had little effect on JET compared with the IR FP, suggesting differences in mechanism of action between the two regions. The electrode catheter and pacing device developed here at George Washington University could potentially be used in humans for rate control of JET and AF in the near future.

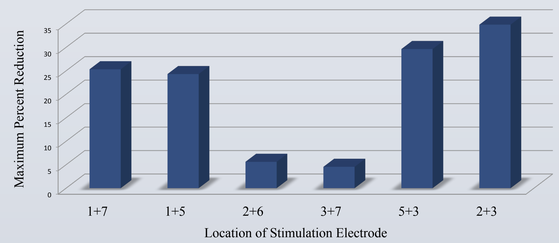

Figure 4. Heart rate reduction following selective site stimulation of the inferior right fat pad. Multiple sites of the inferior right fat pad were stimulated using combinations of electrodes and the ventricular rate (VR) response was assessed. Simultaneous stimulation of electrodes 2 and 3 produced the greatest reduction in heart rate with a maximum percent VR reduction of 34.8%.

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